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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/675,226	09/29/2003	Tony Romeo	14233.10USU1	1700

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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/675,226	ROMEO ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-32 and 36-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/12/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-45 are pending. Claims 1-32 and 36-45 have been withdrawn as being drawn to non-elected inventions. Claims 33-35 are currently under examination.

Election/Restrictions

Applicant's election with traverse of Group XVI in the response filed 5/10/2006 is acknowledged. The traversal is on the ground(s) that it would not be unduly burdensome to search the claims of Groups X, XI, XII, XIII, and XVI since these groups are classified in the same class and subclass. This is not found persuasive for the reasons set forth below.

First, the classification system has no statutory recognition regarding whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct patented inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.01). In the instant situation, the inventions of Groups I-XIX are drawn to distinct inventions which are related as separate products capable of separate manufacture, use, or sale as described in the previous Office Action. Restriction between the inventions is deemed to be proper for the reasons previously set forth.

In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. The literature search, particularly relevant in this art, is not co-extensive in scope, because, for example, the claims are drawn to methods of inhibiting three different proteins. Additionally, it is submitted that the inventions of Groups I-XIX have acquired a separate status in the art. Clearly different searches and issues are involved in the examination of each Group.

The requirement is still deemed proper and is therefore made FINAL.

Specification

The use of the trademark Sephadex has been noted on page 16 in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

It should be noted that the cited occurrence of improper use is only exemplary and applicant should review the specification to correct any other use of trademarks.

Information Disclosure Statement

The information disclosure statement filed 1/12/2004 has been considered. An initialed copy is enclosed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of

guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claims are drawn to methods of reducing adhesin synthesis in biofilm-forming bacteria; reducing β-1,6-N-acetylglucosamine polymer synthesis; or reducing glycosyltransferase activity in biofilm-forming bacteria, each comprising reducing YcdQ activity. The claims encompass reducing the synthesis of all adhesins (not just the polysaccharide intercellular adhesin (PIA) discussed in the specification) as well as reducing all glycosyltransferase activity (not just YcdQ activity). The claims also encompass all biofilm-forming bacteria (which includes both gram positive and gram negative species such as *Staphylococcus epidermidis, E. coli, and Pseudomonas aeruginosa*)

Guidance of the specification/The existence of working examples: The specification provides no working examples of methods of reducing YcdQ activity. Assays for determining the activity of enzyme inhibitors and screening for inhibitors are disclosed; and it is suggested that analogues, synthetic compounds, or known glycosyltransferase inhibitors such as tunicamycin, bacitracin, isofagomine, or azafagomine can be used to inhibit ycd proteins. However, the results of such assays are not presented and no specific method steps (with demonstrated efficacy) for reducing YcdQ activity are claimed or disclosed in the specification. Moreover, the disclosure in the specification, with regard to specific means of reducing YcdQ activity is entirely prophetic and is totally lacking with regard to the specific method steps that engender a given "means". There is also no guidance in the specification regarding how a reduction in YcdQ activity would lead to a reduction in the synthesis of adhesins other than PIA,

to a reduction in the activity of glycosyltransferases other than YcdQ, or to a reduction in β-1,6-N-acetylglucosamine polymer synthesis.

State of the art: There is very little information in the art about YcdQ. As disclosed in the specification, YcdQ is an N-acetylglucosaminyltransferase that catalyzes the conversion of UDP-acetylglucosamine to β-1,6-N-acetylglucosamine. Though there is no evidence to suggest that YcdQ can be found in any organism other than *E. coli*, there are similar enzymes in other species. The IcaA protein in *Staphylococcus epidermidis* and *Staphylococcus aureus* is an N-acetylglucosaminyltransferase that catalyzes the synthesis of PIA from UDP-acetylglucosamine (Cramton *et al.*, Infect. Immun., 67:5427-5433, 1999). However, of the four "known glycosyltransferase inhibitors" disclosed in the specification, tunicamycin and bacitracin were found by Gerke *et al.* not to affect the synthesis of PIA by the IcaA protein (J. Biol. Chem., 273:18586-18593, 1998, see abstract).

Accordingly, one of skill in the art would have no reason to believe that one could reduce YcdQ activity by any means in any organism other than *E. coli*. Further, the specification and the claims lack method steps for reducing YcdQ activity, and one of skill in the art would not know how to reduce YcdQ activity, especially when one considers that two of the four possible inhibitors mentioned by the specification as known glycosyltransferases were unable to inhibit PIA synthesis. In view of the lack of support in the art and specification for methods of reducing adhesin synthesis in biofilm-forming bacteria, reducing β-1,6-N-acetylglucosamine polymer synthesis, or reducing glycosyltransferase activity in biofilm-forming bacteria, by reducing YcdQ activity, it would require undue experimentation on the part of the skilled artisan to make and use the vaccine as claimed; therefore, the claims are not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: active steps to reduce YcdQ activity.

Claims 35 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 is rendered vague and indefinite by the phrase "reducing glycosyltransferase activity in biofilm-forming bacteria, comprising reducing YcdQ activity." YcdQ is a glycosyltransferase; therefore, it is unclear how reducing glycosyltransferase activity will reduce glycosyltransferase activity.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Davis *et al.* (Microbiology, Harper and Row Publishers, USA, 1968).

The instant claims are drawn to methods of reducing adhesin synthesis in biofilm-forming bacteria; reducing β-1,6-N-acetylglucosamine polymer synthesis; or reducing glycosyltransferase activity in biofilm-forming bacteria, each comprising reducing YcdQ activity.

Davis *et al.* disclose a method of killing *E. coli* by contacting cells with 0.01 N HCl for 40 minutes (see page 345, paragraph bridging columns 1-2). Killing cells would necessarily reduce YcdQ activity and therefore reduce adhesin synthesis, β-1,6-N-acetylglucosamine polymer synthesis, and glycosyltransferase activity.

Conclusion

No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Gangle whose telephone number is 571-272-1181. The examiner can normally be reached on M-F 8:00 am - 4:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Brian Gangle
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ROBERT A. ZEMAN
PRIMARY EXAMINER